

I. AMENDMENTS

IB. AMENDMENTS TO THE CLAIMS

Cancel claim 8 without prejudice to renewal.

1. (Canceled)
2. (Previously presented) A method for obtaining a mammalian cell comprising a genomic deletion in a range of from about 50 kb to about 3000 kb, which method comprises the steps of:
 - a) modifying the genome of mammalian cells comprising a wild-type target locus by introducing a construct comprising two regions of sequences that are homologous to the 5' and 3' flanking sequences of said wild-type target locus, wherein said homologous sequences are at least about 500 base pairs;
 - b) identifying cells containing said deletion by selecting cells containing a selectable marker present in said construct; and
 - c) recovering mammalian cell comprising said deletion.
3. (Previously presented) The method of claim 2 wherein said target locus is an HPRT locus.
4. (Previously presented) The method of claim 2 wherein said target locus is an MHC Class I locus.
5. (Previously presented) The method of claim 2 wherein said target locus is an MHC Class II locus.
6. (Previously presented) The method of claim 2 wherein said target locus is an immunoglobulin locus.
7. (Previously presented) The method of claim 2 wherein said mammalian cell is selected from the group consisting of the islets of Langerhans, adrenal medulla cells, osteoblasts, osteoclasts,

epithelial cells, endothelial cells, B lymphocytes, T lymphocytes, neurons, glial cells, ganglion cells, retinal cells, keratinocytes, embryonic stem (ES) cells, liver cells, bone marrow cells, and muscle cells.

8.-10. (Canceled)

11. (Previously presented) A method for preparing a mammalian cell deficient in hypoxanthine phosphoribosyltransferase (HPRT), which method comprises introducing into target cells containing a wild-type HPRT locus a construct which comprises a modified DNA fragment, said fragment corresponding to the genomic site at which the wild-type HPRT locus is located,

wherein said DNA fragment comprises a first sequence immediately downstream of the second exon of the *hprt* locus congruent with the wild-type sequence 55 kb upstream of said first sequence in the native DNA containing wild-type HPRT locus, wherein a mammalian cell deficient in HPRT is obtained.

12. (Original) The method of claim 11 which further comprises the steps of

- a) identifying cells containing said deletion by selecting cells containing a selectable marker present in said construct; and
- b) recovering cells containing said deletion.

13.-15. (Canceled)